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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,584	10/31/2003	Phillip B. Messersmith	7317	1890

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EXAMINER	
KOSSON, ROSANNE	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,584	MESSERSMITH ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *14-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,12 and 13* is/are rejected.

7)☒ Claim(s) *9-11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/31/03 & 9/2/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' election of Group I, claims 1-13, in the reply filed on April 13, 2006 is acknowledged. Because Applicants have not indicated that their election was made with traverse, and because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election is considered to have been made **without** traverse (see MPEP § 818.03(a)). Claims 14-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions, there being no allowable generic or linking claim. No claims have been amended, canceled or added.

The restriction requirement is still deemed proper and is therefore made FINAL. Accordingly, claims 1-13 are examined on the merits herewith.

Allowable Subject Matter

Claims 9-11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims (claims 1 and 8). The prior art does not reasonably teach or suggest a biomimetic gelation system comprising a polymeric acyl donor peptide comprising at least two contiguous glutaminyl residues, a polymeric acyl acceptor peptide comprising a lysine residue, and transglutaminase in which at least one of the polymers comprises PEG. The prior art does not reasonably teach or suggest adding a PEG component to polypeptides containing at least two contiguous glutaminyl residues or a lysine residue and that are linked by transglutaminase to form a biomimetic gel. See Sperinde et al., discussed below, who disclose PEG-based

hydrogels for cell and tissue culture that are linked by transglutaminase, but who do not disclose polymers containing PEG and K or PEG and two contiguous Q residues.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 2 recites that the acyl donor peptide comprises two to "about five" glutaminyl residues. "About five" is not defined in the specification, and Applicants' intended meaning with respect to the number of glutaminyl residues in the claimed donor peptide cannot be determined, rendering the metes and bounds of the claims unclear. Applicants may wish to delete the word "about." Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Labroo et al. (US 5,428,014). Labroo et al. disclose a biomimetic gelation system comprising a transglutaminase, an acyl donor peptide comprising at least two contiguous glutaminyl (glutamine) residues (SEQ ID NO: 1 or SEQ ID NO: 2), and an acyl acceptor peptide comprising a lysine residue (one SEQ ID NOS: 1-4). See col. 1, line 63, to col. 4, line 43. These three

reagents react to form biomaterials that are stable, biodegradable matrices that can be used to produce tissue adhesives, wound repair formulations, rigid prosthetic devices, bone or soft tissue matrices or carriers for controlled-release drug compositions (see col. 2, lines 12-27, and col. 4, line 38, to col. 5, line 5). These peptides can be cross-linked by transglutaminase and used in a variety of polymer formulations to add stability to the biomaterial created and enable the biomaterial to adhere to tissue surfaces (see col. 2, lines 38-43). Each peptide from among SEQ ID NOS: 1-4 is a polymer, an amino acid polymer, and is conjugated by the action of transglutaminase to other peptide sequences. The glutaminyl (Q) residues in SEQ ID NO: 1 (acyl donor peptide) may be conjugated to the lysine residue in SEQ ID NOS: 1-4 (acyl acceptor peptides). The glutaminyl (Q) residues in SEQ ID NO: 2 (acyl donor peptide) may be conjugated to the lysine residue in SEQ ID NOS: 1-4 (acyl acceptor peptides). Therefore, a holding of anticipation is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Labroo et al. (US 5,428,014) in view of Sperinde et al. ("Synthesis and characterization of enzymatically-cross-linked poly(ethylene glycol) hydrogels," Macromolecules 30:5255-5264, 1997), Benedict et al. (US 4,908,404), and Richardson et al. (US 5,490,980). The teachings of Labroo et al. are discussed above. Labroo et al. do not disclose peptides that are conjugated to the polymer PEG (poly(ethylene glycol)), peptides that comprise a DOPA residue or peptides in which the K residue is adjacent to L or F. Labroo et al. also do not disclose that the transglutaminase is isolated from guinea pig liver or a bacterium.

Sperinde et al. disclose a biomimetic gelation system comprising transglutaminase, an acyl donor peptide comprising PEG (poly(ethylene glycol)) and one glutamine/glutaminyl residue (Q or GQG), and an acyl acceptor peptide comprising the polymer K-F (lysine and phenylalanine residues) and a K residue directly adjacent to an F residue (see p. 5255, p. 5256, 2^{d} full paragraph, and p. 5257, 3^{d} and 4th full paragraphs). F directly following K increases the transglutaminase reaction rate (see p. 5258, right col., 1st paragraph). The transglutaminase is from guinea pig liver, the most well characterized and readily available transglutaminase and the one with the broadest substrate specificity (see p. 5258, left col., last paragraph). PEG is a hydrophilic, gel-forming polymer for cell-based therapeutics and tissue engineering that is biocompatible, relatively inert and widely used (see p. 5255, 1st paragraph and right col.). PEG-based hydrogels that are formed by enzymatic cross-linking offer the potential for kinetic control of the gelation process and may be used to form gels in situ (by extrusion or injection) and gels that form highly hydrated networks around living cells (see abstract). These gels may contain multifunctional PEG macromers that have ligands for cell interactions (see paragraph bridging

pp. 5261-5262), and the PEG stabilizes the protein moieties in the gels (see p. 5257, right col., 3[d] paragraph). Thus, Sperinde et al. disclose PEG-based hydrogels for cell and tissue culture that are linked by transglutaminase, but they do not disclose polymers containing PEG and K or PEG and two contiguous Q residues.

Regarding claim 5, one of ordinary skill in the art at the time that the invention was made would have been motivated to place an F residue next to a K residue in the acyl acceptor peptide because Sperinde et al. teach that F directly following K increases the transglutaminase reaction rate (see p. 5258, right col., 1[st] paragraph).

Regarding claims 3 and 6, Benedict et al. disclose that incorporating DOPA groups and lysine residues, which are positively charged or cationic, into a polypeptide improves the adhesion of the polypeptide to cells or tissue (see col. 3, line 36, to col. 4, line 39; col. 5, lines 6-30; and col. 7, lines 35-40). Thus, one of ordinary skill in the art at the time that the invention was made would have been motivated to incorporate DOPA groups (in addition to the K residues already present) into the polypeptide portion of the polymers used to form the biomimetic gels in order to improve the adhesion of the gels to their respective tissue sites, because Labroo et al. teach that their biomimetic gels are used as tissue adhesives, wound repair formulations, prosthetic devices, bone or soft tissue matrices or carriers for controlled-release drug compositions, gels that need to adhere to the site at which they are applied in order to work, and Benedict et al. disclose that DOPA improves bioadhesion.

Regarding claim 6, the sequences DOPA-L-K, DOPA-F-K, K-L-DOPA and K-F-DOPA are not associated with any particular result or effect in the hydrogels produced with polymers containing these polypeptides. The significance of including K-F and DOPA is discussed above (increased transglutaminase reaction and increased tissue adherence). Therefore, to one of ordinary skill in the art, these arrangements represent two obvious choices among alternative

polypeptide sequences containing K-F and DOPA that are conjugated to PEG. On p. 14 of the specification, Applicants have presented data from their kinetics experiments comparing the kinetic constants for the polypeptides DOPA-K-G, DOPA-F-K-G and DOPA-L-K-G to those of five other polypeptides. But only eight polypeptides of 2-4 amino acids were tested, and the claim recites a very large genus of polypeptides, any acyl acceptor polypeptide comprising one of the sequences DOPA-L-K, DOPA-F-K, K-L-DOPA or K-F-DOPA. As a result, any special properties that these sequences confer have not been demonstrated.

Regarding claim 13, Richardson et al. disclose that transglutaminase is produced by bacteria, as well as by mammalian cells, and that transglutaminase from a bacterial source, a species of *Streptoverticillum*, is commercially available and inexpensive. Transglutaminase from any organism performs the same reaction, the coupling of lysine and glutamine residues (see col. 10, lines 59-67). Thus, one of ordinary skill in the art would have been motivated to use a bacterial transglutaminase in the biomimetic gelation systems discussed above, because Richardson et al. disclose that transglutaminases from any organism are functionally equivalent and that a bacterial transglutaminase is inexpensive and commercially available.

In view of the foregoing, a holding of obviousness is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rosanne Kosson
Examiner, Art Unit 1653

rk/2006-04-25

Rosanne Kosson

Jon Weber
Supervisory Patent Examiner